L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:464267 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 131:116517
TITLE: Preparation of N-acyl-phenylalanine derivatives as inhibitors of α4-mediated cell adhesion
INVENTOR(S): Sircar, Ila; Gudmundsson, Kristjan S.; Martin, Richard
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936393	A1	19990722	WO 1999-US993	19990119
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2318527	A1	19990722	CA 1999-2318527	19990119
CA 2318527	C	20061017		
AU 9924584	A	19990802	AU 1999-24584	19990119
AU 749568	B2	20020627		
BR 9907040	A	20001017	BR 1999-7040	19990119
EP 1049662	A1	20001108	EP 1999-904115	19990119
EP 1049662	B1	20060621		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2002509131	T	20020326	JP 2000-540111	19990119
JP 3634749	B2	20050330		
NZ 506081	A	20030228	NZ 1999-506081	19990119
TW 591007	B	20040611	TW 1999-88100776	19990119
SG 118147	A1	20060127	SG 2002-4434	19990119
AT 330935	T	20060715	AT 1999-904115	19990119
PT 1049662	T	20060929	PT 1999-904115	19990119
ES 2264252	T3	20061216	ES 1999-904115	19990119
US 6521666	B1	20030218	US 2000-619712	20000719
MX 2000PA07138	A	20010328	MX 2000-PA7138	20000720
HK 1029979	A1	20061110	HK 2001-100247	20010110
US 20030191118	A1	20031009	US 2002-286777	20021104
US 6855843	B2	20050215		
JP 2005002116	A	20050106	JP 2004-202046	20040708

PRIORITY APPLN. INFO.:

US 1998-71840P	P	19980120
JP 2000-540111	A3	19990119
WO 1999-US993	W	19990119
US 2000-619712	A3	20000719

OTHER SOURCE(S): MARPAT 131:116517
GI For diagram(s), see printed CA Issue.

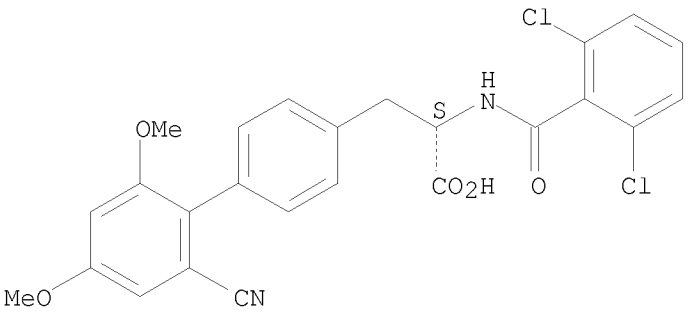
AB The present invention relates to a pharmaceutical composition comprising as an active ingredient a compound of formula [I; wherein ring A is an aromatic or a heterocyclic ring; Q is a bond, carbonyl, lower alkylene optionally substituted by HO or Ph, lower alkenylene, or -O-(lower alkylene)-; n is 0, 1 or 2; Z is oxygen or sulfur; W is oxygen, sulfur, -CH:CH-, -NH- or -N:CH-; R1, R2 and R3 are the same or different and are hydrogen, halogen, hydroxyl, a substituted or unsubstituted lower alkyl group, a substituted or unsubstituted lower alkoxy group, a substituted or unsubstituted amino group, CO2H or an amide or an ester thereof, cyano, lower alkylthio, lower alkanesulfonyl, substituted or unsubstituted SO2NH2, etc.; R4 is tetrazolyl, carboxyl group, amide or ester; R5 is hydrogen, nitro, amino, hydroxyl, lower alkanoyl, lower alkyl, etc.; R6 is selected from (a) a substituted or unsubstituted Ph group, (b) a substituted or unsubstituted pyridyl group, (c) a substituted or unsubstituted thienyl group, (d) a substituted or unsubstituted benzofuranyl group, etc.; or a pharmaceutically acceptable salt thereof]. These phenylalanine derivs. are useful for treating or preventing conditions caused by α4-mediated cell adhesion such as rheumatoid arthritis, asthma, psoriasis, eczema, contact dermatitis and other skin inflammatory diseases, diabetes, multiple sclerosis, systemic lupus erythematosus (SLE), inflammatory bowel disease including ulcerative colitis and Crohn's disease, and other diseases involving leukocyte infiltration of the gastrointestinal tract, or other epithelial lined tissues, such as skin, urinary tract, respiratory airway, and joint synovium. N-(tert-butoxycarbonyl)-O-(trifluoromethanesulfonyl)-L-tyrosine Me ester (preparation given) was coupled with 2-methoxybenzene boronic acid in toluene/DMF in the presence of K2CO3 and Pd(PPh3)4 at 80 °C for 24 h to give N-(tert-butoxycarbonyl)-4-(2-methoxyphenyl)-L-phenylalanine Me ester. The latter compound was treated with CF3CO2H in CH2Cl2 for 1.5 h to remove the Boc group and then condensed with 2,6-dichlorobenzoyl chloride in the presence of diisopropylethylamine at room temperature for 24 h to give N-(2,6-dichlorobenzoyl)-4-(2-methoxyphenyl)-L-phenylalanine Me ester (II) which was saponified with LiOH in THF/MeOH at room temperature for 3 h, evaporated, treated with H2O, adjusted Ph 2, and extracted with EtOAc to give N-(2,6-dichlorobenzoyl)-4-(2-methoxyphenyl)-L-phenylalanine (III). II and III in vitro inhibited at IC50 of 1≥ and 0.3≥ μM, resp., β7-mediated cell adhesion which measured the adhesive interactions of a B-cell line, RPMI, known to express α4β7, to the alternatively spliced region of fibronectin referred to as CS-1, in the presence of test compds.

IT 232272-83-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-acyl-phenylalanine derivs. as inhibitors of α4-mediated cell adhesion for prevention and treatment of diseases caused by α4-mediated cell adhesion)

RN 232272-83-2 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 2'-cyano-α-[(2,6-dichlorobenzoyl)amino]-4',6'-dimethoxy-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT